

**Amendments to the Drawings**

The attached sheets of drawings include changes to Figure 2 and Figure 6. These sheets replace the original sheets including Figure 2 and Figure 6. In both Figure 2 and Figure 6, the corresponding SEQ ID NOs have been added.

Attachment: Replacement Sheets  
Annotated Sheets Showing Changes

## **REMARKS**

In the present amendment, claims 1, 5, 6, 16 and 29 have been amended. Claim 16 has been canceled. The amendments to the claims are supported throughout the specification, in the claims and in the sequence listing. In addition, the specification has been amended at page 10 to indicate that the patent or application file contains at least one drawing executed in color as required under 37 CFR § 1.84, and to correct a typographical error on page 46. No new matter is believed to be added.

After entry of these amendments, claims 1-3, 5-15, 17-27 and 29-39 are pending.

### **Drawings/Specification**

The drawings stand objected to under 37 CFR § 1.83(a) because Figures 3 and 7 purportedly fail to show the colors as described in the Brief Description of the Figures. Applicants respectfully submit that the as-filed figures included two color figures: FIGS. 3 and 7. Submitted herewith is a Petition under 37 CFR § 1.84 requesting acceptance of these color drawings.

In addition, the specification stands objected to for referencing an attorney docket number. Applicants have removed this reference. Withdrawal of this objection is requested.

The specification also stands objected to for containing sequence disclosures that fail to comply with the requirements set forth in 37 CFR § 1.821. Applicants have amended the specification to include the corresponding SEQ ID NOs for the sequences on page 96. The Examiner also alleges that Tables I-V represent linear amino acid sequence disclosures, and, therefore, need a heading identifying the protein name and its corresponding SEQ ID NO. Applicants have amended the specification accordingly although they respectfully point out that Table II does not correlate to a SEQ ID NO so only a descriptive title has been added. Applicants have also amended claim 1 so that it recites SEQ ID NO:1 and points out that SEQ ID NO:1 and SEQ ID NO:13 are the same sequence. Additionally, Applicants have amended Figures 2 and 6 to include the proper corresponding SEQ ID NOs. Replacement drawings and Annotated drawings showing the changes are enclosed herein. Applicants have also amended the specification on page 10 to correct the corresponding SEQ ID NOs in the figure legend.

The Examiner has also objected to the specification for containing hyperlinks. Applicants have amended the specification to remove the hyperlinks on pages 22 and 96. Withdrawal of this objection is requested.

**Rejection of claims 1 and 5 under 35 U.S.C. § 101**

The Examiner has rejected claims 1 and 5 as allegedly being directed to non-statutory subject matter without requiring the performance of a result outside of a computer or representing some type of physical transformation which is concrete or tangible. That rejection is respectfully traversed to the extent the rejection is applied to the claims as amended.

Applicants have amended claims 1 and 5 to include the step of screening the chemical entity in an assay that characterizes binding to said GR Site II in order to comply with 35 U.S.C. § 101. Applicants respectfully request reconsideration by the Examiner and withdrawal of this rejection.

**Rejection of claims under 35 U.S.C. § 112, second paragraph**

Claims 1, 5-10, 16, 27 and 29 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. That rejection is respectfully traversed to the extent the rejection is applied to the claims as amended

(a) The Examiner alleges that the phrase “any part of the cavity” in claim 1, 6 and 29, and the phrase “any part of” in claim 5, renders the claims indefinite. Applicants have amended these phrases to read “the cavity” and “said GR Site II,” respectively. By this amendment, Applicants believe that they have obviated this rejection.

(b) The Examiner alleges that the amino acid residues in claims 1, 5, 6, 27 and 29 do not match the amino acid sequence of SEQ ID NO:13 as well as those in Figure 2. Applicants have amended the specification on page 10 and Figure 2 so that the SEQ ID NOs correspond accurately. Additionally, Applicants have amended claim 1 to refer to SEQ ID NO:1. Support for this amendment can be found throughout the specification, for example on page 96, lines 15-31. By this amendment, Applicants believe that they have obviated this rejection.

(c) The Examiner alleges that the phrase “human GR; rat GR...” in claim 16 renders the claim indefinite. Applicants have amended claim 16 to include the corresponding SEQ ID NOs

as defined in Figure 6. By this amendment, Applicants believe that they have obviated this rejection.

(d) The Examiner has rejected claims 7-10 under 35 U.S.C. § 112, second paragraph, as they are dependent upon rejected independent claims. As the independent claims have been amended to overcome the Examiner's rejections, Applicants believe that the rejection of claims 7-10 has been overcome as well.

**Rejection of claims under 35 U.S.C. § 102(e) and § 103(a)**

The Examiner has rejected claims 1, 5-10, 16, 27 and 29 under 35 U.S.C. § 102(e) and § 103(a) as allegedly being anticipated by or, in the alternative, as obvious over US patent 6,965,850 (hereinafter "'850").

It is well settled that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP §2131 (quoting *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Id.* (quoting *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)). Therefore, '850 must describe each and every element of claims 1, 5 and 6 in order to anticipate these claims under Section 102(b).

Applicants respectfully submit that '850 does not teach each and every element of the claims. Amended claims 1, 5, 6 and 29 are directed to methods for evaluating the potential of a chemical entity to bind to a GR Site II, methods of designing a ligand of a GR Site II, methods for identifying modulators of a GR, and methods of identifying a ligand of a GR Site II, respectively. Amended claims 1, 5, 6 and 29 also recite that the GR Site II is comprises the amino acids E537-V543, L566, G567, Q570-W577, S599-A607, W610, R611, R614, Q615, P625, Y663, L664 and K667 and is defined by the structure coordinates according to Table 1. Amended claim 1 also recites the structure coordinates according to Tables, III-V.

In contrast to the instant invention, '850 describes the use of compounds binding to the co-activator binding site of NHRs which is not Site II. Site II of the instant invention is situated on almost the opposite side of the protein from the Site II that is disclosed in '850. In addition, Site II of the instant invention comprises a different amino acid sequence than that disclosed for the Site II disclosed in '805. Site II of '850 comprises amino acids V571, I572, A574, V575,

A578, K579, F584, Q592, M593, L596, Q597, W600, E751, M752, and E755-I757 which are different from Site II of the instant invention. Further, the structural coordinates disclosed in '850 are different than those recited in the instant claims. Because '850 teaches neither the Site II nor its structural coordinates recited in the instant claims, it does not teach every element of the claims 1, 5 and 6, as amended, or of dependent claims 7-10, 27 and 29, and, therefore, does not anticipate the instant claims. Thus, Applicants respectfully request reconsideration by the Examiner and withdrawal of this rejection.

Claims 1, 5-10, 16, 27 and 29 also stand rejected under §103(a) as being unpatentable over '850. As discussed above, Applicant submits that '850 does not disclose the subject matter of the claims 1, 5 and 6, as amended, nor claims 7-10, 27 and 29 that ultimately depend therefrom. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

The Examiner has also rejected claims 1, 5-10, 16, 27 and 29 under 35 U.S.C. § 103(a) as being unpatentable over WO 00/52050 (hereinafter "'050") in view of US Patent 5,856,116 (hereinafter "'116").

Amended claims 1, 5 and 6 are directed to methods for evaluating the potential of a chemical entity to bind to GR Site II, wherein said GR Site II is a structure described by the structure coordinates of amino acids E537-V543, L566, G567, Q570-W577, S599-A607, W610, R611, R614, Q615, P625, Y663, L664 and K667 of SEQ ID NO:1 according to Table I, Table III, Table IV or Table V. These structure coordinates are not disclosed in either '050 or '116. As such, Applicants submit that '050 does not disclose the subject matter of the claims 1, 5 and 6, as amended, nor claims 7-10, 27 and 29 that ultimately depend therefrom and, therefore, do not render these claim obvious. Applicants respectfully submit that '116 does not cure the deficiencies of '050, and that accordingly the combination of '050 and '116 does not suggest Applicants' claimed invention. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

The Examiner has also rejected claims 1, 5-10, 16, 27 and 29 under 35 U.S.C. § 103(a) as being unpatentable over US Patent Application Publication No. 2005/0181362 (hereinafter "'362"). Specifically, the Examiner alleges that '362 teaches the crystallization of the complex of GR ligand binding with two ligands and the determination of the three-dimensional structure by the X-ray diffraction method.

Amended claims 1, 5 and 6 are directed to methods for evaluating the potential of a chemical entity to bind to GR Site II, wherein said GR Site II is a structure described by the structure coordinates of amino acids E537-V543, L566, G567, Q570-W577, S599-A607, W610, R611, R614, Q615, P625, Y663, L664 and K667 of SEQ ID NO:1 according to Table I, Table III, Table IV or Table V. These structure coordinates are not disclosed in '362. As such, Applicants submit that '362 does not disclose the subject matter of the claims 1, 5 and 6, as amended, nor claims 7-10, 27 and 29 that ultimately depend therefrom and, therefore, do not render these claim obvious. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

**Rejection of claims 1, 5-10, 16, 27 and 29 under 35 U.S.C. § 103(a) over '362 in view of '850**

The Examiner has rejected claims 1, 5-10, 16, 27 and 29 under 35 U.S.C. § 103(a) as being unpatentable over '362 in view of '850. For the foregoing reasons, '362 does not does not disclose the subject matter of the claims 1, 5 and 6, as amended, nor claims 7-10, 27 and 29 that ultimately depend therefrom and, therefore, do not render these claim obvious. Applicants respectfully submit that '850 does not cure the deficiencies of '362, and that accordingly the combination of '362 and '850 does not suggest Applicants' claimed invention. Applicants request reconsideration and withdrawal of this rejection.

**CONCLUSION**

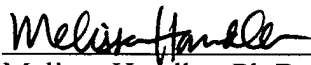
In view of the foregoing amendments and remarks, allowance of the application is respectfully requested. The Examiner is invited to contact the undersigned if there are any questions concerning the prosecution of this application.

Appl. No. 10/621,807  
Docket No. D0250 NP

The Commissioner is authorized to charge Deposit Account 19-3880 (Bristol-Myers Squibb Company) for any requisite fees due or to credit any overpayment.

Respectfully submitted,

Bristol-Myers Squibb Company  
Patent Department  
P.O. Box 4000  
Princeton, NJ 08543-4000  
609-252-4323



Melissa Handler, Ph.D.  
Agent for Applicants  
Reg. No. 52,988

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# ANNOTATED SHEET

FIGURE 2 (continued)

RXRalpha	306	WNELLIASFS	HRSTAV....	..KDGILLAT	GL...HVHRN	..S...AHSAG	VG.....
RARgamma	267	CLDILMLRIC	TRY...TPE.	..QDTMTFSD	GL...TLNRT	..Q..MH...	..NAGF....
PR	755	WMSLMVFGLG	WRSYK....H	VSGQMLYFAP	DL...ILNEQ	..R..MKESS	FY.....
AR	742	WMGLMVFAMG	WRSFT....N	VNSRMLYFAP	DL...VFNEY	..RM.HKSRM	Y.....
ERalpha	382	WLEILMIGLV	WRSME.....	..HPGKLLFAP	NL...LLDRN	..Q.GKCV	VEG MV.....
ERbeta	331	WMEVLMMGLM	WRSID.....	..HPGKLIFAP	DL...VLDRD	..E.GKCV	VEG IL.....
VitDR	216	AIEVIMLRSN	ESF...TMD.	...DMSWTCG	N.QDYKYRVS	..D..VT...	..KAGH....
PPARgamma	322	VHEIIYTMLA	SLM...NK..	...DGVLISE	GQ...GFMTR	E.F..LK...	.....SLRK
MR	806	WMCLSSFALS	WRSYK....H	TNSQFLYFAP	DL...VFNEE	..KM..HQSAM	YE.....
TRbeta	301	CMEIMSLRAA	VRY...DPE.	..SETLTLNG	EM...AVTRG	..Q..LK...	..NGGL....
GR	600	WMFLMAFALG	WRSYR....Q	SSANLLCFAP	DL...INEQ	..R...MTLPC	MY.....
RXRalpha	345	...A.IF.DR	VLTELVS KMR	DMQMDKTELG	CLRAIVL.FN	PDSKG...LS	.....
RARgamma	305	..GP.LT.DL	VFAFAGQLL	PLEMDDTETG	LLSAICL.IC	GDRMD...LE	.....
PR	796	...S.LC.LT	MWQIPQEFV	KLOVSQEEFL	CMKVLLL.LN	.TIP.LEGLR	.....
AR	783	...S.QC.VR	MRHLSQEFG	WLQITPQEFL	CMKALLL.FS	.IIP.VDGLK	.....
ERalpha	422	...E.IF.DM	LLATSSRFR	MMNLQGEFV	CLKSIILLNS	.GV.....	YTF.LSSTLK
ERbeta	371	...E.IF.DM	LLATTSRFR	ELKLQHKEYL	CVKAMILLNS	.....	...LVTAT.Q
VitDR	255	..SLELI.EP	LIKFOVGLK	KLNLHEEEHV	LLMAICI.VS	PDRPG...VQ	.....
PPARgamma	359	PFGD.FM.EP	KFEFAVKFN	ALELDDSDLA	IFTAVII.LS	GDRPG...LL	.....
MR	848	...L..C.QG	MHQISLQFV	RLQLTFFEYT	IMKVLLL.LS	.TIP.KDGLK	.....
TRbeta	339	..GV.VS.DA	IFDLGMSLS	SFNLDDTEVA	LLQAVLL.MS	SDRPG...LA	.....
GR	641	...D..QCKH	MLYVSSELH	RLQVSYYEYL	CMKTLLL.LS	.SVP.KDGLK	.....
RXRalpha	386	...NPAEVEA	LREKVYASLE	AYCKH..KYP	EQPG.....	...RFAKLLL	RLPALRSIGL
RARgamma	336	...EPEKVDK	LQEPLLEALR	LYARR..RRP	SQPY.....	...MFPRMLM	KITDLRGIST
PR	837	...SQTQFEE	MRSSYIRELI	KAIG...LRQ	K...GVV..S	SSQRFYQLTK	LLDNLHDLVK
AR	824	...NQKFDE	LRMNYIKELD	RIIA...CKR	K...NPT..S	CSRRFYQLTK	LLDSVQPIAR
ERalpha	467	SLEEKDHIHR	VLDKITDTLI	HLMA...KAG	L...TLQ..Q	QHERLAQLLL	ILSHIRHMSN
ERbeta	411	DADSSRKLAH	LLNAVTDALV	WVIA...KSG	I...SSQ..Q	QSMRLANLLM	LLSHVRHASN
VitDR	297	...DAALIEA	IQDRLSNTLQ	TYIRC..RHP	PP.L.....	...LYAKMIQ	KLADLRSLNE
PPARgamma	402	...NVKPIED	IQDNLLQALE	LQLKL..NHP	ESSQ.....	...LFAKLLQ	KMTDLRQIVT
MR	888	...SQAAFEE	MRTNYIKELR	KMVT.KCPNN	S...G....Q	SWQRFYQLTK	LLDSMHDLS
TRbeta	380	...CVERIEK	YQDSFLLAFE	HYINY..RKH	HVTH.....	...FWPKLLM	KVTDLRMIGA
GR	681	...SQELFDE	IRMTYIKELG	KAIV...KRE	G...N..SSQ	NWQRFYQLTK	LLDSMHEVVE
RXRalpha	432	KCLEHLFFFK	LIGDTPIDTF	LMEMLEAPHQ	MT.....	.....	.....
RARgamma	382	KGAERA....	.....	.....	...ITLKMEI	PGP...MPP	LIREMLENP.
PR	886	QLHLYC....	.....	.....	.....	.....	.....L
AR	873	ELHQFT....	.....	.....	.....	.....	.....F
ERalpha	519	KGMEHL....	.....	.....	.....	.....	.....Y
ERbeta	463	KGMEHL....	.....	.....	.....	.....	.....L
VitDR	342	EHSKQY....	.....	.....	...RCLSFQP	ECSMK..LTP	LVLEVFG...
PPARgamma	448	EHVQLL....	.....	.....	..QVIKKTET	DMS....LHP	LLQEIKYKDL
MR	937	DLLEFC....	.....	.....	.....	.....	.....F
TRbeta	426	CHASRF....	.....	.....	...LHMKVEC	PT...ELFPP	LFLEVFE...
GR	730	NLLNYC....	.....	.....	.....	.....	.....F



# ANNOTATED SHEET

FIGURE 6

u87951 Squirrel	MDSKESLTP.	GKEENPSSVL	TQERGNVMDL	CKILRGGATL	KVSVSSTSLA
AF141371 Pig	.....	.....	.....	.....	.....
l13196 Guinea Pig	MDLKESVTSS	..KEVPSSVL	GSERRNVIDF	YKTVRGGATV	KVSASSPSLA
u87953 Marmoset	MDSKESLTP.	GKEENPSSVL	TQERGNVMDL	CKILRGGATL	KVSVSSTSLA
u87952 Ma'z Monkey	MDSKESLTP.	GKEENPSSVL	TQERGNVMDL	SKILRGGATL	KVSVSSTSLA
Human	MDSKESLTP.	GREENPSSVL	AQERGDVMDL	YKTLRGGATV	KVSASSPSLA
m14053 rat	MDSKESLAPP	GRDEVPGSLL	GQGRGSVMDL	YKSLRGGATV	KVSASSPSVA
x04435 mouse	MDSKESLAPP	GRDEVPGSLL	GRGRGSVMDL	YKTLRGGATV	KVSASSPSVA
u87951 Squirrel	AASQSDSKQQ	RLLVDFPKGS	VSNAQQ....	.....	.....PDLs
AF141371 Pig	.....	.VSASSPSLA	AVSQPDSKQQ	RLAVDFPKGS	GSNAQQPDLs
l13196 Guinea Pig	AAAQSDSKQR	RLLVDFPKGS	GSNAQQ....	.....	.....PDLs
u87953 Marmoset	AASQSDSKQQ	RLLVDFPKGS	VSNAQQ....	.....	.....PDLs
u87952 Ma'z Monkey	AASQSDSKQQ	RLLVDFPKGS	VSNAQQ....	.....	.....PDLs
Human	VASQSDSKQR	RLLVDFPKGS	VSNAQQ....	.....	.....PDLs
m14053 rat	AASQADSKQQ	RILLDFSKGS	TSNVQQRQQQ	QQQQQQQQQQ	QQQQQQPGLs
x04435 mouse	AASQADSKQQ	RILLDFSKGS	ASNAQQ....	.....QQ	QQQQQPDLs
u87951 Squirrel	KAVSLSMGLY	MGETETKVMG	NDLGFPQQGQ	ISLSSGETDL	QLLEESIANL
AF141371 Pig	KAVSLSMGLY	MGETETKVMG	SDLGFPQQGQ	ISLSSGETDF	RLLEESIANL
l13196 Guinea Pig	KAVSLSMGLY	MGETETKVMG	NDLGFPQQGQ	ISLPSGETDF	RLLEESIANL
u87953 Marmoset	KAVSLSMGLY	MGETETKVMG	NDLGFPQQGQ	ISLSSGETDL	QLLEESIANL
u87952 Ma'z Monkey	KAVSLSMGLY	MGETETKVMG	NDLGFPQQGQ	ISLSSGETDL	QLLEESIANL
Human	KAVSLSMGLY	MGETETKVMG	NDLGFPQQGQ	ISLSSGETDL	KLLEESIANL
m14053 rat	KAVSLSMGLY	MGETETKVMG	NDLGYPQQGQ	LGLSSGETDF	RLLEESIANL
x04435 mouse	KAVSLSMGLY	MGETETKVMG	NDLGYPQQGQ	LGLSSGETDF	RLLEESIANL
u87951 Squirrel	NRSTSVPENP	KSSASSSVSA	APKEKEFPKT	HSDVSSEQQN	LKGQTGSNGG
AF141371 Pig	SRSTSVPENP	KSSASAAGPA	APA EKAFPKT	HSDGAPEQPN	VKGQTGTNGG
l13196 Guinea Pig	SRSTSVPENP	KNSASA.VSG	TPTE.EFPKT	QSDLSSEQEN	LKSQAGTNGG
u87953 Marmoset	NRSTSVPENP	KSSASSSVSA	APKEKEFPKT	HSDVSSEQQN	LKGQTGTNGG
u87952 Ma'z Monkey	NRSTSVPENP	KSSASSSVSA	APKEKEFPKT	HSDVSSEQQN	LKGQTGTNGG
Human	NRSTSVPENP	KSSASTAVSA	APTEKEFPKT	HSDVSSEQQH	LKGQTGTNGG
m14053 rat	NRSTSVPENP	KSSTSATGCA	TPTEKEFPKT	HSDASSEQQN	RKSQTGTNGG
x04435 mouse	NRSTSRPENP	KSSTPAAGCA	TPTEKEFPQT	HSDPSSEQQN	RKSQPGTNGG
u87951 Squirrel	NVKLYTADQS	TFDI....LQ	DLEFSSGSPG	KETNQSPWKS	DLLIDENCLL
AF141371 Pig	NVKLFTTDQS	TFDIWRKKLQ	DLELPSGSPG	KETSESPWSS	DLLIDENCLL
l13196 Guinea Pig	NVK.FPPDQS	TFDI....LK	DLEFSSGSPG	KERSESPWRP	DLLMDESCLL
u87953 Marmoset	NAKLCTADQS	TFDI....LQ	DLEFSSGSPG	KETNQSPWRS	DLLIDENCLL
u87952 Ma'z Monkey	NVKLYTADQS	TFDI....LQ	DLEFSSGSPG	KETNQSPWRS	DLLIDENCLL
Human	NVKLYTTDQS	TFDI....LQ	DLEFSSGSPG	KETNESPWRS	DLLIDENCLL
m14053 rat	SVKLYPTDQS	TFDL....LK	DLEFSAGSPS	KDTNESPWRS	DLLIDEN.LL
x04435 mouse	SVKLYTTDQS	TFDI....LQ	DLEFSAGSPG	KETNESPWRS	DLLIDEN.LL

# ANNOTATED SHEET

## FIGURE 2

RXRalpha	225	S.....	ANEDM.....	.....	.....	PVE.RILEAE	LAVE.PKTET
RARgamma	182	L.....	SPQ..LEE..	.....	.....	LIT.KVSKAH	QETF.P....
PR	682	.....	.....Q.	.....LI.	.....P	PLINLLMSIE	..PD.V....
AR	669	.....	.....	.....C	Q.....P	IFLNVLEAIE	..PG.V....
ERalpha	305	.....	.....	.....	SLALSLTAD	QMVSALLDAE	..PP.I....
ERbeta	261	.....	.....	.....	DALSPE	QLVLTLEAE	..PP.H....
VitDR	120	.LRPKL....	SEE..QQR..	.....	.....	IIA.ILLDAH	HKTY.D....
PPARgamma	207	E.....	SAD..LRA..	.....	.....	LAK.HLYDSY	IKSF.P....
MR	731	.....	.....S	RA.....LT.	.....P	SPVMVLENIE	..PE.I....
TRbeta	211	.....KPEP	TDE..EWE..	.....	.....	LIK.TVTEAH	VATNAQ....
GR	523	.....	.....	..ATLPQLT.	.....P	TLVSLLEVIE	..PE.V....
RXRalpha	249	YVEANMGLNP	SSPNDPVTN.	.....	.....IC.	.....	.....
RARgamma	203	.....	.....	.....	.....S	LCQL.GKYTT	N.....
PR	699	.....	.....I	YAGHDNTKPD	TSSSLTTS..	.....	.....
AR	685	.....	.....V	CAGHDNNQPD	SFAALLSS..	.....	.....
ERalpha	327	.....	.....L	YSEYDPTPRF	SEASMMGL..	.....	.....
ERbeta	281	.....	.....V	LISR.....	TEASMMMS..	.....	.....
VitDR	145	.....	.....	.....	.....P	.....	..TYSDFCQFR
PPARgamma	.....	.....	.....	.....	.....	.....	.....
MR	750	.....	.....V	YAGYDSSKPD	TAENLLST..	.....	.....
TRbeta	236	.....	.....	.....	.....G	SHWKQKRKFL	P.....
GR	544	.....	.....L	YAGYDSSVPD	STWRIMTT..	.....	.....
RXRalpha	.....	.....	.....	.....	.....	.....	.....
RARgamma	214	..SSADHRVQ	L.....	.....	.....	.....	.....
PR	.....	.....	.....	.....	.....	.....	.....
AR	.....	.....	.....	.....	.....	.....	.....
ERalpha	.....	.....	.....	.....	.....	.....	.....
ERbeta	.....	.....	.....	.....	.....	.....	.....
VitDR	155	PPVRV.....	.NDGGGSVTL	ELS.....	.....	.....	.....
PPARgamma	228	.....	.....	...LTKAKAR	AILTGKTTDK	SPFVIYDMNS	LMMGEDKIKF
MR	.....	.....	.....	.....	.....	.....	.....
TRbeta	248	..EDIGQAPK	V.....	.....	.....	.....	.....
GR	.....	.....	.....	.....	.....	.....	.....
RXRalpha	271	.....	.....	..Q...AADK	QLFTLVEWAK	RIPHFSELPL	DDQVILLRAG
RARgamma	223	.....	...DLGLWDK	FSE...LATK	CIKIVEFAK	RLPGFTGLSI	ADQITLLKAA
PR	718	.....	.....	...LNQLGER	QLLSVVKWSK	SLPGFRNLHI	DDQITLIQYS
AR	705	.....	.....	...LNELGER	QLVHVVKWAK	ALPGFRNLHV	DDQMAVIQYS
ERalpha	345	.....	.....	...LTNLADR	ELVHMINWAK	RVPGFVDLTL	HDQVHLLLECA
ERbeta	294	.....	.....	...LTKLADK	ELVHMISWAK	KIPGFVELSL	FDQVRLLESC
VitDR	172	.....	...QLSMLPH	LAD...LVSY	SIQKVIGFAK	MIPGFRDLTS	EDQIVLLKSS
PPARgamma	265	KHITPLQEQS	KEVAIRIFQG	CQF...RSVE	AVQEITEYAK	SIPGFVNLDL	NDQVTLLKYG
MR	769	.....	.....	...LNRLAGK	OMIQVVKWAK	VLPGFKNLPL	EDQITLIQYS
TRbeta	257	.....	...DLEAFSH	FTK...IITP	AITRVVDFAK	KLPMFCELPC	EDQIILLKGC
GR	563	.....	.....	...LNMLGGR	QVIAAVKWAK	AIPGFRNLHL	DDQMTLLQYS

# ANNOTATED SHEET

**FIGURE 2 (continued)**

RXRalpha		.....	.....	.....	.....	.....	.....	.....	.....
RARgamma		.....	.....	.....	.....	.....	.....	.....	.....
PR	893	.NTFIQSRAL	SVEFPPEMMSE	VIAAQLPKIL	AGMVKPLLFFH	K.....	.....	.....	.....
AR	880	.DLLIKSHMV	SVDFPEMMAE	IISVQVPKIL	SGKVKPIYFH	T.....	.....	.....	.....
ERalpha	526	.SMKCKNV..	.....	.....	.....	.VPLYDLLLE	ML.....	.....	.....
ERbeta	470	NMKC.....	.....	.....	.....	.....	..KNVVPVYD	.....	.....
VitDR		.....	.....	.....	.....	.....	.....	.....	.....
PPARgamma		.....	.....	.....	.....	.....	.....	.....	.....
MR	944	.YTFRESHAL	KVEFPAMLVE	IISDQLPKVE	SGNAKPLYFH	R.....	.....	.....	.....
TRbeta		.....	.....	.....	.....	.....	.....	.....	.....
GR	737	.QTFLDKTMS	IEFPEMLAEI	ITNQIPKYSN	GNIKKLLFHQ	K.....	.....	.....	.....
RXRalpha		.....	.....	(SEQ ID NO:3)					
RARgamma		.....	.....	(SEQ ID NO:4)					
PR		.....	.....	(SEQ ID NO:5)					
AR		.....	.....	(SEQ ID NO:6)					
ERalpha		.....	.....	(SEQ ID NO:7)					
ERbeta	482	LLLEMLNAHV	LR...	(SEQ ID NO:8)					
VitDR		.....	.....	(SEQ ID NO:9)					
PPARgamma	477	.....	..Y..	(SEQ ID NO:10)					
MR	984	.....	...K.	(SEQ ID NO:11)					
TRbeta	453	.....	....D	(SEQ ID NO:12)					
GR		.....	.....	(SEQ ID NO:13)					

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FIGURE 6 (Continued)

u87951 Squirrel	SPLAGEEDSF	LLEGNSNEDC	KPLILPDTKP	KIKDNGDLVL	SSSSNVTLPQ
AF141371 Pig	SPLAGEEDPF	LLEGSTEDC	KPLVLPDTKP	KVKDNGELIL	PSPNSVPLPQ
113196 Guinea Pig	SPLAGEDDPF	LLEGNSNEDC	KPLILPDTKP	KIKDNGDGIL	SSSNSVPQPQ
u87953 Marmoset	SPLAGEEDSF	LLEGNSNEDC	KPLILPDTKP	KIKDNGDLVL	SSSSNVTLPQ
u87952 Ma'z Monkey	SPLAGEEDSF	LLEGNSNEDC	KPLILPDTKP	KIKDNGDLVL	SSSSNVTLPQ
Human	SPLAGEDDSF	LLEGNSNEDC	KPLILPDTKP	KIKDNGDLVL	SSPSNVTLPQ
m14053 rat	SPLAGEDDPF	LLEGNTNEDC	KPLILPDTKP	KIKDTGDTIL	SSPSSVALPQ
x04435 mouse	SPLAGEDDPF	LLEGDVNEDC	KPLILPDTKP	KIQDTGDTIL	SSPSSVALPQ

u87951 Squirrel	VKTEKEDFIE	LCTPGVIKQE	KLSTVYCQAS	FPGANIIGNK	MSAISIHGVS
AF141371 Pig	VKTEKEDFIE	LCTPGVIKQE	KLGPAYCQAS	FSGANIIGGK	MSAISVHGVS
113196 Guinea Pig	VKIGKEDFIE	LCTPGVIKQE	KLGPVYCQAS	FSGANIIGNK	MSAISVHGVS
u87953 Marmoset	VKTEKEDFIE	LCTPGVIKQE	KLSTVYCQAS	FPGANIIGNK	MSAISIHGVS
u87952 Ma'z Monkey	VKTEKEDFIE	LCTPGVIKQE	KLSTVYCQAS	FPGANVIGNK	MSAISIHGVS
Human	VKTEKEDFIE	LCTPGVIKQE	KLGTVYCQAS	FPGANIIGNK	MSAISVHGVS
m14053 rat	VKTEKDDFIE	LCTPGVIKQE	KLGPVYCQAS	FSGTNIIGNK	MSAISVHGVS
x04435 mouse	VKTEKDDFIE	LCTPGVIKQE	KLGPVYCQAS	FSGTNIIGNK	MSAISVHGVS

u87951 Squirrel	TSGGQMYHYD	MNTA.SLSQQ	QDQKPIFNVI	PPIPVGSENV	NRCQGSDDN
AF141371 Pig	TSGGQLYHYD	MNTAASLSKQ	QEOKPLFNVI	PPIPVGSENV	NRCQGSDDN
113196 Guinea Pig	TSGGQMYHYD	MNTA.SLSQQ	QDQKPIFNVI	PPIPVGSENV	NRCQGSDDN
u87953 Marmoset	TSGGQMYHYD	MNTA.SLSQQ	QDQKPIFNVI	PPIPVGSENV	NRCQGSDDN
u87952 Ma'z Monkey	TSGGQMYHYD	MNTA.SLSQQ	QDQKPIFNVI	PPIPVGSENV	NRCQGSDDN
Human	TSGGQMYHYD	MNTA.SLSQQ	QDQKPIFNVI	PPIPVGSENV	NRCQGSDDN
m14053 rat	TSGGQMYHYD	MNTA.SLSQQ	QDQKPVFNVI	PPIPVGSENV	NRCQGSDDN
x04435 mouse	TSGGQMYHYD	MNTA.SLSQQ	QDQKPVFNVI	PPIPVGSENV	NRCQGSDDN

u87951 Squirrel	LTSLGTLNFP	GRTVFSNGYS	SPSMRPDVSS	PPSSSSTAT	GPPPKLCLVC
AF141371 Pig	LTSLGTLNFS	GRSVFSNGYS	SPGMRPDVSS	PPSSSSAAT.	GPPPKLCLVC
113196 Guinea Pig	LTSLGTVNFP	GRSVFSNGYS	SPGLRPDVSS	PPSSSST.TT	GPPPKLCLVC
u87953 Marmoset	LTSLGTLNFP	GRTVFSNGYS	SPSMRPDVSS	PPSSSSTAT	GPPPKLCLVC
u87952 Ma'z Monkey	LTSLGTLNFP	GRTVFSNGYS	SPSMRPDVSS	PPSSSSTAT	GPPPKLCLVC
Human	LTSLGTLNFP	GRTVFSNGYS	SPSMRPDVSS	PPSSSSTAT	GPPPKLCLVC
m14053 rat	LTSLGALNFP	GRSVFSNGYS	SPGMRPDVSS	PPSSSSAAT.	GPPPKLCLVC
x04435 mouse	LTSLGAMNFA	GRSVFSNGYS	SPGMRPDVSS	PPSSSSTAT.	GPPPKLCLVC

u87951 Squirrel	SDEASGCHYG	VLTCGSCKVF	FKRAVEGQHN	YLCAGRNDIC	IDKIRRKNC
AF141371 Pig	SDEASGCHYG	VLTCGSCKVF	FKRAVEGQHN	YLCAGRNDIC	IDKIRRKNC
113196 Guinea Pig	SDELSGCHYG	VLTCGSCKVF	FKRAVEGQHN	YLCAGRNDIC	IDKIRRENCP
u87953 Marmoset	SDEASGCHYG	VLTCGSCKVF	FKRAVEGQHN	YLCAGRNDIC	IDKIRRKNC
u87952 Ma'z Monkey	SDEASGCHYG	VLTCGSCKVF	FKRAVEGQHN	YLCAGRNDIC	IDKIRRKNC
Human	SDEASGCHYG	VLTCGSCKVF	FKRAVEGQHN	YLCAGRNDIC	IDKIRRKNC
m14053 rat	SDEASGCHYG	VLTCGSCKVF	FKRAVEGQHN	YLCAGRNDIC	IDKIRRKNC
x04435 mouse	SDEASVCHYG	VLTCGSCKVF	FKRAVEGQHN	YLCAGRNDIC	IDKIRRKNC

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## FIGURE 6 (Continued)

u87951 Squirrel	ACRYRKCLQA	GMNLEARKTK	KKIKGIQQAT	TGVSQETSEN	PANKTIVPAT
AF141371 Pig	ACRYRKCLQA	GMNLEARKTK	KKIKGIQQAT	TGVSQETSEN	SANKTIVPAT
l13196 Guinea Pig	ACRYRKCLQA	GMNLQARKTK	KKIKGIQQAT	TGVSQNTSEN	P.NKTIVPAT
u87953 Marmoset	ACRYRKCLQA	GMNLEARKTK	KKIKGIQQAT	TGVSQETSEN	PANKTIVPAT
u87952 Ma'z Monkey	ACRYRKCLQA	GMNLEARKTK	KKIKGIQQAT	TGVSQETSEN	PANKTIVPAT
Human	ACRYRKCLQA	GMNLEARKTK	KKIKGIQQAT	TGVSQETSEN	PGNKTIVPAT
m14053 rat	ACRYRKCLQA	GMNLEARKTK	KKIKGIQQAT	AGVSQDTSN	P.NKTIVPAA
x04435 mouse	ACRYRKCLQA	GMNLEARKTK	KKIKGIQQAT	AGVSQDTSN	.ANKTIVPAA

u87951 Squirrel	525	LPQLTPTLVS	LLEVIEPEVL	YAGYDSTVPD	STWRIMTTLN	MLGGROVIAA
AF141371 Pig	489	LPQLTPTLVS	LLEVIEPEVL	YAGYDSSIPD	STWRIMTALN	MLGGROVIAA
l13196 Guinea Pig	519	LPQLTPTLVS	LLEVIEPEVI	HSGYDSTSPD	STWRIMTTLN	MLGGROVIAA
u87953 Marmoset	525	LPQLTPTLVS	LLEVIEPEVL	YAGYDSTVPD	STWRIMTTLN	MLGGROVIAA
u87952 Ma'z Monkey	525	LPQLTPTLVS	LLEVIEPEVL	YAGYDSTVPD	STWRIMTTLN	MLGGROVIAA
Human	525	LPQLTPTLVS	LLEVIEPEVL	YAGYDSSVPD	STWRIMTTLN	MLGGROVIAA
m14053 rat	543	LPQLTPTLVS	LLEVIEPEVL	YAGYDSSVPD	SAWRIMTTLN	MLGGROVIAA
x04435 mouse	531	LPQLTPTLVS	LLEVIEPEVL	YAGYDSSVPD	SAWRIMTTLN	MLGGROVIAA

u87951 Squirrel	575	VKWAKAIPGF	RNLHLDDQMT	LLQYSWMFLM	AFALGWRSYR	QASSNLLCFA
AF141371 Pig	539	VKWAKAIPGF	RNLHLDDQMT	LLQYSWMFLM	VFALGWRSYR	QSSASLLCFA
l13196 Guinea Pig	569	VKWAKAIPGF	RNLHLDDQMT	LLQYSWMFLM	AFALGWRSYK	QSNGLLCFA
u87953 Marmoset	575	VKWAKAIPGF	RNLHLDDQMT	LLQYSWMFLM	AFALGWRSYR	QASSNLLCFA
u87952 Ma'z Monkey	575	VKWAKAIPGF	RNLHLDDQMT	LLQYSWMFLM	AFALGWRSYR	QASSNLLCFA
Human	575	VKWAKAIPGF	RNLHLDDQMT	LLQYSWMFLM	AFALGWRSYR	QSSANLLCFA
m14053 rat	593	VKWAKAILGL	RNLHLDDQMT	LLQYSWMFLM	AFALGWRSYR	QSSGNLLCFA
x04435 mouse	581	VKWAKAIPGF	RNLHLDDQMT	LLQYSWMFLM	AFALGWRSYR	QASGNLLCFA

u87951 Squirrel	625	PDLIINEQRM	TLPCMYDQCK	HMLYVSSELH	RLQVSYEYYL	CMKTLLLLSS
AF141371 Pig	589	PDLVINEQRM	ALPCMYDQCR	HMLYVSSELQ	RLQVSYEYYL	CMKTLLLLSS
l13196 Guinea Pig	619	PDLIINEQRM	SLPWMYDQCR	YMLYVSSELK	RLQVSYEYYL	CMKTLLLLSS
u87953 Marmoset	625	PDLIINEQRM	TLPCMYDQCK	HMLYVSSELH	RLQVSYEYYL	CMKTLLLLSS
u87952 Ma'z Monkey	625	PDLIINEQRM	TLPCMYDQCK	HMLYVSSELH	RLQVSYEYYL	CMKTLLLLSS
Human	625	PDLIINEQRM	TLPCMYDQCK	HMLYVSSELH	RLQVSYEYYL	CMKTLLLLSS
m14053 rat	643	PDLIINEQRM	SLPCMYDQCK	HMLFVSSELQ	RLQVSYEYYL	CMKTLLLLSS
x04435 mouse	631	PDLIINEQRM	TLPCMYDQCK	HMLFISTELQ	RLQVSYEYYL	CMKTLLLLSS

u87951 Squirrel	VPKDGLKSQE	LFDEIRMTYI	KELGKAIVKR	EGNSSQNWQR	FYQLTKLLDS
AF141371 Pig	VPKDGLKSQE	LFDEIRMTYI	KELGKAIVKR	EGNSSQNWQR	FYQLTKLLDS
l13196 Guinea Pig	VPKEGLKSQE	LFDEIRMTYI	KELGKAIVKR	EGNSSQNWQR	FYQLTKLLDS
u87953 Marmoset	VPKDGLKSQE	LFDEIRMTYI	KELGKAIVKR	EGNSSQNWQR	FYQLTKLLDS
u87952 Ma'z Monkey	VPKDGLKSQE	LFDEIRMTYI	KELGKAIVKR	EGNSSQNWQR	FYQLTKLLDS
Human	VPKDGLKSQE	LFDEIRMTYI	KELGKAIVKR	EGNSSQNWQR	FYQLTKLLDS
m14053 rat	VPKEGLKSQE	LFDEIRMTYI	KELGKAIVKR	EGNSSQNWQR	FYQLTKLLDS
x04435 mouse	VPKEGLKSQE	LFDEIRMTYI	KELGKAIVKR	EGNSSQNWQR	FYQLTKLLDS

# ANNOTATED SHEET

## FIGURE 6 (Continued)

u87951 Squirrel	MHEVVENLLN	YCFQTFLDKT	MSIEFPEMLA	EIITNQLPKY	SNGNIKKLLF
AF141371 Pig	MHDVVENLLN	YCFQT.....	.....	.....	.....
113196 Guinea Pig	LHEIVGNLLN	ICFKTFLDKT	MNIEFPEMLA	EIITNQLPKY	SNGDIKKLLF
u87953 Marmoset	MHEVVENLLN	YCFQTFLDKT	MSIEFPEMLA	EIITNQLPKY	SNGNIRKLLF
u87952 Ma'z Monkey	MHEVVENLLN	YCFQTFLDKT	MSIEFPEMLA	EIITNQLPKY	SNGNIKKLLF
Human	MHEVVENLLN	YCFQTFLDKT	MSIEFPEMLA	EIITNQIPKY	SNGNIKKLLF
m14053 rat	MHEVVENLLT	YCFQTFLDKT	MSIEFPEMLA	EIITNQIPKY	SNGNIKKLLF
x04435 mouse	MHDVVENLLS	YCFQTFLDKS	MSIEFPEMLA	EIITNQIPKY	SNGNIKKLLF

u87951 Squirrel	HQK	<u>(SEQ ID NO:14)</u>
AF141371 Pig	...	<u>(SEQ ID NO:15)</u>
113196 Guinea Pig	HQK	<u>(SEQ ID NO:16)</u>
u87953 Marmoset	HQK	<u>(SEQ ID NO:17)</u>
u87952 Ma'z Monkey	HQK	<u>(SEQ ID NO:18)</u>
Human	HQK	<u>(SEQ ID NO:19)</u>
m14053 rat	HQK	<u>(SEQ ID NO:20)</u>
x04435 mouse	HQK	<u>(SEQ ID NO:21)</u>